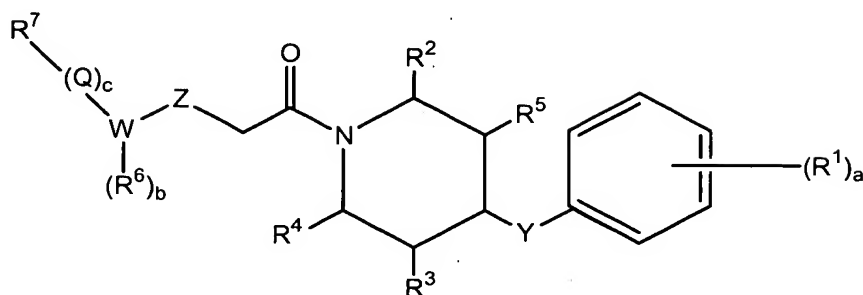


CLAIMS

What is claimed is:

1. A compound of the formula



or pharmaceutically acceptable salts, tautomers, and pro-drugs thereof; wherein

a is 1, 2, 3, 4 or 5;

b is 0, 1, 2, 3, or 4;

c is 0 or 1;

Q is (C₁-C₆)alkyl;

W is (C₆-C₁₀)aryl or (C₂-C₉)heteroaryl;

Y is oxygen, or NR⁸ wherein R⁸ is hydrogen or (C₁-C₆)alkyl;

Z is oxygen or NR⁹, where R⁹ is hydrogen, (C₁-C₆)alkyl, or acetyl;

each R¹ is independently selected from the group consisting of: hydrogen,

halo, cyano, nitro, trifluoromethyl, trifluoromethoxy, (C₁-C₆)alkyl, hydroxy, (C₁-C₆)alkylcarbonyloxy, and (C₁-C₆)alkoxy;

R², R³, R⁴ and R⁵ are each independently hydrogen or (C₁-C₆)alkyl optionally substituted with 1 to 3 halo groups;

each R⁶ is independently selected from a list consisting of: hydrogen, halo,

(C₁-C₆)alkyl optionally substituted with 1 to 3 halo groups; cyano, (C₁-C₆)alkoxy, aminocarbonyl, carboxy, (C₁-C₆)alkylcarbonyl, or (C₁-C₆)alkoxy optionally substituted by 1 to 3 halo groups; and

R⁷ is selected from a list consisting of hydrogen, halo, (C₁-C₆)alkyl optionally substituted with 1 to 3 halo groups, [(C₁-C₆)alkyl]₂amino(C₁-C₆)alkylaminocarbonyl, amino(C₁-C₆)alkylaminocarbonyl, (C₁-C₆)alkylamino(C₁-C₆)alkylaminocarbonyl, cyano, (C₁-C₆)alkoxy, aminocarbonyl, (C₁-C₆)alkylaminocarbonyl, [(C₁-C₆)alkyl]₂aminocarbonyl, (C₁-C₆)alkylsulfonylamino, (C₁-C₆)alkylsulfonylaminocarbonyl, ureido, aminosulfonyl, [(C₁-C₆)alkyl]₂aminosulfonyl,

- (C₁-C₆)alkylaminosulfonyl, [(C₁-C₆)alkyl]₂aminocarbonyl(C₁-C₆)alkylaminocarbonyl, (C₁-C₆)alkylaminocarbonyl(C₁-C₆)alkylaminocarbonyl, aminocarbonyl(C₁-C₆)alkylaminocarbonyl, (C₁-C₆)alkylsulfonylamino, hydroxy(C₁-C₆)alkylcarbonylamino, ureido(C₁-C₆)alkylaminocarbonyl, [(C₁-C₆)alkyl]₂ureido(C₁-C₆)alkylaminocarbonyl, (C₁-C₆)alkylureido(C₁-C₆)alkylaminocarbonyl, (C₂-C₉)heteroarylaminocarbonyl, carboxy, (C₁-C₆)alkoxy(C₁-C₆)alkyl(C₂-C₉)heterocyclecarbonyl, (C₂-C₉)heterocyclecarbonyl, hydroxy(C₂-C₉)heterocyclecarbonyl, aminocarbonyl(C₂-C₉)heterocyclecarbonyl, carboxy(C₂-C₉)heterocyclecarbonyl, amino(C₂-C₉)heteroaryl(C₁-C₆)alkyl, (C₁-C₆)alkylamino(C₂-C₉)heteroaryl(C₁-C₆)alkyl, [(C₁-C₆)alkyl]₂amino(C₂-C₉)heteroaryl(C₁-C₆)alkyl, (C₂-C₉)heteroarylaminocarbonyl(C₁-C₆)alkoxy, (C₁-C₆)alkylsulfonylamino(C₁-C₆)alkoxy, aminocarbonyl(C₁-C₆)alkoxy, carboxy(C₁-C₆)alkoxy, aminosulfonyl, (C₁-C₆)alkylcarbonylaminosulfonyl, hydroxy(C₁-C₆)alkylcarbonylaminosulfonyl, (C₁-C₆)alkoxycarbonylaminosulfonyl, (C₁-C₆)alkoxy(C₁-C₆)alkylcarbonylaminosulfonyl, hydroxysulfonyl, hydroxy, hydroxy(C₁-C₆)alkylaminocarbonyl, carboxy(C₂-C₉)heterocycloxy or [carboxy][amino](C₁-C₆)alkoxy, aminocarbonyl(C₁-C₆)alkylcarbonylamino, (C₁-C₆)alkylaminocarbonyl(C₁-C₆)alkylcarbonylamino, [(C₁-C₆)alkyl]₂aminocarbonyl(C₁-C₆)alkylcarbonylamino, amino(C₁-C₆)alkylcarbonylamino, (C₁-C₆)alkylamino(C₁-C₆)alkylcarbonylamino, [(C₁-C₆)alkyl]₂amino(C₁-C₆)alkylcarbonylamino, ureido(C₁-C₆)alkylcarbonylamino, (C₁-C₆)alkylureido(C₁-C₆)alkylcarbonylamino, [(C₁-C₆)alkyl]₂ureido(C₁-C₆)alkylcarbonylamino, amino(C₁-C₆)alkylsulfonylamino, amino(C₁-C₆)alkylcarbonylaminosulfonyl, (C₁-C₆)alkylamino(C₁-C₆)alkylcarbonylaminosulfonyl, [(C₁-C₆)alkyl]₂amino(C₁-C₆)alkylcarbonylaminosulfonyl, aminosulfonylamino, (C₁-C₆)alkylaminosulfonylamino, [(C₁-C₆)alkyl]₂aminosulfonylamino, (C₂-C₉)heterocycloxy, (C₂-C₉)heteroaryloxy, (C₂-C₉)heterocycleamino, (C₂-C₉)heteroarylaminocarbonyl, amino(C₁-C₆)alkoxy, (C₁-C₆)alkylamino(C₁-C₆)alkoxy, [(C₁-C₆)alkyl]₂amino(C₁-C₆)alkoxy, amino(C₁-C₆)alkylamino, (C₁-C₆)alkylcarbonylamino(C₁-C₆)alkylamino, ureido(C₁-C₆)alkylamino, hydroxy(C₁-C₆)alkylamino, (C₁-C₆)alkoxy(C₁-C₆)alkylamino, and (C₁-C₆)alkylsulfonylamino(C₁-C₆)alkylamino;

with the proviso that at least one of R², R³, R⁴, and R⁵ is (C₁-C₆)alkyl.

2. A compound according to claim 1, wherein R¹ is halo; a is 1 or 2; Y is oxygen; Z is oxygen; W is phenyl; b is 0, 1 or 2 and R⁶ is selected from a list consisting of halo, (C₁-C₆)alkyl, cyano, and (C₁-C₆)alkylcarbonyl.

5 3. A compound according to claim 1, wherein R¹ is halo; a is 1 or 2; Y is oxygen; Z is oxygen or NH; W is pyridyl; b is 0, 1 or 2 and R⁶ is selected from a list consisting of halo, (C₁-C₆)alkyl, cyano, and (C₁-C₆)alkylcarbonyl.

10 4. A compound according to claim 1, wherein c is 0, and R⁷ is selected from a list consisting of (C₁-C₆)alkylsulfonylamino, (C₁-C₆)alkylaminocarbonyl, aminosulfonyl, aminocarbonyl(C₁-C₆)alkylaminocarbonyl, (C₁-C₆)alkylaminocarbonyl, hydroxy(C₁-C₆)alkylcarbonylamino, aminocarbonylamino, carboxy(C₂-C₉)heterocycloalkoxy, carboxy(C₂-C₉)heteroarylcarbonyl, ureido(C₁-C₆)alkylaminocarbonyl, [(C₁-C₆)alkyl]₂amino(C₁-C₆)alkylaminocarbonyl, (C₁-C₆)alkylsulfonylaminocarbonyl(C₁-C₆)alkoxy, aminocarbonyl(C₁-C₆)alkoxy, and carboxy(C₁-C₆)alkoxy.

15 5. A compound according to claim 1, wherein c is 1, and R⁷ is selected from a list consisting of (C₁-C₆)alkylsulfonylaminocarbonyl(C₁-C₆)alkoxy, (C₂-C₉)heteroarylaminocarbonyl(C₁-C₆)alkoxy, and (C₁-C₆)alkylsulfonylaminocarbonyl.

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6. A compound according to claim 1, wherein R² and R³ are both methyl groups and R⁴ and R⁵ are both hydrogen.

25 7. A compound according to claim 2, wherein R² and R³ are methyl; R⁴ and R⁵ are hydrogen; R² and R³ are trans; Y and R³ are trans; W is phenyl; c is 0; and R⁷ is selected from the group consisting of: (C₁-C₆)alkylsulfonylamino, (C₁-C₆)alkylaminocarbonyl, aminosulfonyl, aminocarbonyl(C₁-C₆)alkylaminocarbonyl, (C₁-C₆)alkylaminocarbonyl, hydroxy(C₁-C₆)alkylcarbonylamino, aminocarbonylamino, carboxy(C₂-C₉)heterocycloalkoxy, carboxy(C₂-C₉)heteroarylcarbonyl, ureido(C₁-C₆)alkylaminocarbonyl, [(C₁-C₆)alkyl]₂amino(C₁-C₆)alkylaminocarbonyl, (C₁-C₆)alkylsulfonylaminocarbonyl(C₁-C₆)alkoxy, aminocarbonyl(C₁-C₆)alkoxy, and carboxy(C₁-C₆)alkoxy.

30

8. A compound according to claim 3, wherein R² and R³ are methyl; R⁴ and R⁵ are hydrogen; R² and R³ are trans; Y and R³ are trans; W is pyridyl; c is 0; and R⁷ is selected from the group consisting of: (C₁-C₆)alkylsulfonylamino, (C₁-C₆)alkylaminocarbonyl, aminosulfonyl, aminocarbonyl(C₁-C₆)alkylaminocarbonyl, (C₁-C₆)alkylaminocarbonyl, hydroxy(C₁-C₆)alkylcarbonylamino, aminocarbonylamino, carboxy(C₂-C₉)heterocycloalkoxy, carboxy(C₂-C₉)heteroarylcarbonyl, ureido(C₁-C₆)alkylaminocarbonyl, [(C₁-C₆)alkyl]₂amino(C₁-C₆)alkylaminocarbonyl, (C₁-C₆)alkylsulfonylaminocarbonyl(C₁-C₆)alkoxy, aminocarbonyl(C₁-C₆)alkoxy, and carboxy(C₁-C₆)alkoxy.

10

9. A compound according to claim 2, wherein R² and R³ are methyl; R⁴ and R⁵ are hydrogen; R² and R³ are trans; Y and R³ are trans; W is phenyl; c is 1; and R⁷ is selected from the group consisting of: (C₁-C₆)alkylsulfonylaminocarbonyl(C₁-C₆)alkoxy, (C₂-C₉)heteroarylaminocarbonyl(C₁-C₆)alkoxy, and (C₁-C₆)alkylsulfonylaminocarbonyl.

15

10. A compound according to claim 3, wherein R² and R³ are methyl; R⁴ and R⁵ are hydrogen; R² and R³ are trans; Y and R³ are trans; W is pyridyl; c is 1; and R⁷ is selected from the group consisting of: (C₁-C₆)alkylsulfonylaminocarbonyl(C₁-C₆)alkoxy, (C₂-C₉)heteroarylaminocarbonyl(C₁-C₆)alkoxy, and (C₁-C₆)alkylsulfonylaminocarbonyl.

20

11. A compound according to claim 1, wherein said compound is selected from the group consisting of:

25 2-(4-Chloro-phenoxy)-1-(4-phenoxy-piperidin-1-yl)-ethanone;
2-(4-Chloro-phenoxy)-1-[4-(4-fluoro-phenoxy)-piperidin-1-yl]-ethanone;
5-Chloro-2-{2-[4-(4-fluoro-phenoxy)-piperidin-1-yl]-2-oxo-ethoxy}-benzamide;
(5-Chloro-2-{2-[4-(4-fluoro-phenoxy)-piperidin-1-yl]-2-oxo-ethoxy}-phenyl)-urea;
5-Chloro-2-[(2,4-*cis*)-(2,5-*trans*)-2-[4-(4-fluoro-phenoxy)-2,5-dimethyl-piperidin-1-yl]-2-oxo-ethoxy]-benzamide;
30 [(2,4-*cis*)-(2,5-*trans*)-5-Chloro-2-{2-[4-(4-fluoro-phenoxy)-2,5-dimethyl-piperidin-1-yl]-2-oxo-ethoxy}-phenyl)-acetic acid;
N-[(5-Chloro-2-[(2,4-*cis*)-(2,5-*trans*)-2-[4-(4-fluoro-phenoxy)-2,5-dimethyl-piperidin-1-yl]-2-oxo-ethoxy)-phenyl)-acetyl]-methanesulfonamide;

2-(5-Chloro-2-{2-[(2,4-*cis*)-(2,5-*trans*)-4-(4-fluoro-phenoxy)-2,5-dimethyl-piperidin-1-yl]-2-oxo-ethoxy}-phenyl)-acetamide;

(5-Chloro-2-{2-[4-(4-fluoro-phenoxy)-piperidin-1-yl]-2-oxo-ethoxy}-phenyl)-acetic acid;

5 N-[(5-Chloro-2-{2-[4-(4-fluoro-phenoxy)-piperidin-1-yl]-2-oxo-ethoxy}-phenyl)-acetyl]-methanesulfonamide; and

5-Chloro-2-{2-[(2,4-*cis*)-(2,5-*trans*)-4-(4-fluoro-phenoxy)-2,5-dimethyl-piperidin-1-yl]-2-oxo-ethoxy}-benzamide.

10 12. A pharmaceutical composition for treating or preventing a disorder or condition selected from autoimmune diseases (such as rheumatoid arthritis, Takayasu arthritis, psoriatic arthritis, ankylosing spondylitis, type I diabetes (recent onset), lupus, inflammatory bowel disease, Crohn's disease, optic neuritis, psoriasis, multiple sclerosis, polymyalgia rheumatica, uveitis, thyroiditis and vasculitis); fibrosis
15 (e.g. pulmonary fibrosis (i.e. idiopathic pulmonary fibrosis, interstitial pulmonary fibrosis), fibrosis associated with end-stage renal disease, fibrosis caused by radiation, tubulointerstitial fibrosis, subepithelial fibrosis, scleroderma (progressive systemic sclerosis), hepatic fibrosis (including that caused by alcoholic or viral hepatitis); primary and secondary biliary cirrhosis); allergic conditions (such as
20 asthma, contact dermatitis and atopic dermatitis); acute and chronic lung inflammation (such as chronic bronchitis, chronic obstructive pulmonary disease, adult Respiratory Distress Syndrome, Respiratory Distress Syndrome of infancy, immune complex alveolitis); atherosclerosis; vascular inflammation resulting from tissue transplant or during restenosis (including, but not limited to restenosis following
25 angioplasty and/or stent insertion); other acute and chronic inflammatory conditions (such as synovial inflammation caused by arthroscopy, hyperuremia, or trauma, osteoarthritis, ischemia reperfusion injury, glomerulonephritis, nasal polyposis, enteritis, Behcet's disease, preeclampsia, oral lichen planus, Guillain-Barre syndrome); acute and/or chronic transplant rejection (including xeno-transplantation);
30 HIV infectivity (co-receptor usage); granulomatous diseases (including sarcoidosis, leprosy and tuberculosis); conditions associated with leptin production (such as obesity, cachexia, anorexia, type II diabetes, hyperlipidemia and hypergonadism); Alzheimer's disease; sequelae associated with certain cancers such as multiple myeloma; cancer metastasis, including but not limited to breast cancer; the

production of metalloproteinases and cytokines at inflammatory sites (including but not limited to MMP9, TNF, IL-1, and IL-6) either directly or indirectly (as a consequence of decreasing cell infiltration) thus providing benefit for diseases or conditions linked to these cytokines (such as joint tissue damage, hyperplasia, pannus formation and bone resorption, hepatic failure, Kawasaki syndrome, myocardial infarction, acute liver failure, septic shock, congestive heart failure, pulmonary emphysema or dyspnea associated therewith); tissue damage caused by inflammation induced by infectious agents (such as viral induced encephalomyelitis or demyelination, viral inflammation of the lung or liver (e.g. caused by influenza or hepatitis), gastrointestinal inflammation (for example, resulting from *H. pylori* infection), inflammation resulting from: bacterial meningitis, HIV-1, HIV-2, HIV-3, cytomegalovirus (CMV), adenoviruses, Herpes viruses (Herpes zoster and Herpes simplex) fungal meningitis, lyme disease, malaria) in a mammal, comprising an amount of a compound according to claim 1, or a pharmaceutically acceptable salt thereof, that is effective in treating or preventing such disorder or condition and a pharmaceutically acceptable carrier.

13. A pharmaceutical composition for treating or preventing a disorder or condition that can be treated or prevented by inhibiting MIP-1 α and/or RANTES binding to the receptor CCR1 in a mammal, comprising an amount of a compound according to claim 1, or a pharmaceutically acceptable salt thereof, effective in treating or preventing such disorder or condition and a pharmaceutically acceptable carrier.

14. A method for treating or preventing a disorder or condition selected from autoimmune diseases (such as rheumatoid arthritis, Takayasu arthritis, psoriatic arthritis, ankylosing spondylitis, type I diabetes (recent onset), lupus, inflammatory bowel disease, Crohn's disease, optic neuritis, psoriasis, multiple sclerosis, polymyalgia rheumatica, uveitis, thyroiditis and vasculitis); fibrosis (e.g. pulmonary fibrosis (i.e. idiopathic pulmonary fibrosis, interstitial pulmonary fibrosis), fibrosis associated with end-stage renal disease, fibrosis caused by radiation, tubulointerstitial fibrosis, subepithelial fibrosis, scleroderma (progressive systemic sclerosis), hepatic fibrosis (including that caused by alcoholic or viral hepatitis), primary and secondary biliary cirrhosis); allergic conditions (such as asthma, contact

dermatitis and atopic dermatitis); acute and chronic lung inflammation (such as chronic bronchitis, chronic obstructive pulmonary disease, adult Respiratory Distress Syndrome, Respiratory Distress Syndrome of infancy, immune complex alveolitis); atherosclerosis; vascular inflammation resulting from tissue transplant or during restenosis (including, but not limited to restenosis following angioplasty and/or stent insertion); other acute and chronic inflammatory conditions (such as synovial inflammation caused by arthroscopy, hyperuremia, or trauma, osteoarthritis, ischemia reperfusion injury, glomerulonephritis, nasal polyosis, enteritis, Behcet's disease, preeclampsia, oral lichen planus, Guillian-Barre syndrome); acute and/or chronic transplant rejection (including xeno-transplantation); HIV infectivity (co-receptor usage); granulomatous diseases (including sarcoidosis, leprosy and tuberculosis); conditions associated with leptin production (such as obesity, cachexia, anorexia, type II diabetes, hyperlipidemia and hypergonadism); Alzheimer's disease; sequelae associated with certain cancers such as multiple myeloma; cancer metastasis, including but not limited to breast cancer; the production of metalloproteinases and cytokines at inflammatory sites (including but not limited to MMP9, TNF, IL-1, and IL-6) either directly or indirectly (as a consequence of decreasing cell infiltration) thus providing benefit for diseases or conditions linked to these cytokines (such as joint tissue damage, hyperplasia; pannus formation and bone resorption, hepatic failure, Kawasaki syndrome, myocardial infarction, acute liver failure, septic shock, congestive heart failure, pulmonary emphysema or dyspnea associated therewith); tissue damage caused by inflammation induced by infectious agents (such as viral induced encephalomyelitis or demyelination, viral inflammation of the lung or liver (e.g. caused by influenza or hepatitis), gastrointestinal inflammation (for example, resulting from H. pylori infection), inflammation resulting from: bacterial meningitis, HIV-1, HIV-2, HIV-3, cytomegalovirus (CMV), adenoviruses, Herpes viruses (Herpes zoster and Herpes simplex) fungal meningitis, lyme disease, malaria) in a mammal, comprising administering to a mammal in need of such treatment or prevention an amount of a compound according to claim 1, or a pharmaceutically acceptable salt thereof, that is effective in treating or preventing such disorder or condition.

15. A method for treating or preventing a disorder or condition that can be treated or prevented by antagonizing the CCR1 receptor in a mammal, comprising administering to a mammal in need of such treatment or prevention an amount of a

compound according to claim 1, or a pharmaceutically acceptable salt thereof, that is effective in treating or preventing such disorder or condition.